Twitter Thread by Hilda Bastian, PhD

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@hildabast

Meanwhile, a few days ago the EMA published its EPAR (public assessment report) on the Moderna vax (HT @pajz_) https://t.co/LHW4rGgFwV It's 169 pages ...1/n

...There was "a major objection" to the US manufacturing sites, so they were withdrawn. Complete transfer for Europe to Swiss manufacturing due to conclude soon. (There have been Qs in the US about a batch there https://t.co/g573j7uFNQ)...2/n

> The active substance is manufactured and controlled by Lonza, Visp, Switzerland, with appropriate GMP certification.
>
> Moderna, Norwood, USA is listed with appropriate GMP certification for QC testing until method transfer is completed to Lonza, Visp.
>
> At the time of authorisation, the transfer of 3 methods for the active substance from Moderna, Norwood to Lonza Visp are ongoing to conclude by end of January 2021. The Supervisory Authority, AEMPS confirmed that the GMP certificate issued to Moderna, Norwood, USA for QC testing of the finished product can cover also testing of the active substance for the interim period. A satisfactory protocol for transfer of analytical methods for the active substance has been provided.
>
> Associates of Cape Cod, East Falmouth, MA USA, will be providing endotoxin testing until transfer is complete to Lonza, Visp by end of January 2021.
>
> A major objection was raised regarding US sites proposed for manufacturing of the active substance, these manufacturing sites were subsequently withdrawn from the dossier.

...If you're interested in the chemical & biological aspects of this vaccine, there are pages for you to dig into - not an area I have any expertise in. Small amount of detail of reproductive toxicity study (in rats): no cause for concern....3/n

...The clinical trial data is from November, as for the FDA data. There's more detail than in the FDA report, though, of the phase 2 study, which hasn't been published. 600 people: a lot of data on immunogenicity (but not cell-mediated immunity)...4/n

...More methodological data on blinding etc for the phase 3 trial & *a lot more data* than in the FDA report. And take a moment to appreciate this: 30,000 people enrolled in less than 3 months. Giant thank you's due all round ...5/n

> Enrolment of P301 was completed in less than 3 months on 23 October 2020 with a total of 30,420 randomised participants. The study is since ongoing. Follow-up milestones and corresponding subject

...In my posts, I've pointed to FDA report someone with apparent severe Covid-19 not adjudicated or in Moderna's analyses. Now we know why: no cases before dose 2 & not all suspected ones were adjudicated. That's not reassuring, though they conclude "no substantial bias" ... 6/n

> primary analysis based on adjudicated cases. Analyses based on all adjudicated cases are said to be provided with the final CSR. Overall, no major uncertainties remain that would alter benefit/risk conclusions. However, it cannot be entirely ruled out that some source of bias occurred during case monitoring/processing and that the efficacy estimation may be optimistic to a certain degree.

...Like FDA, EMA point to person with severe Covid-19 in the vaccine group. Overall, data on severity reassured them, but "the cases overall seem mostly mild, which is a limitation of the dataset". "No definitive conclusion on clinical efficacy after one dose can be drawn" ...7/n

...They also conclude the definition of severe Covid-19 "could have been more stringent from a clinical perspective". They say open questions remain about the lower bound for the confidence interval of efficacy, partly because of the case ascertainment issue, so... 8/n

...they want more data in a final report by December 2022 before considering approval. Serious adverse events seem similar to FDA's conclusions (but I haven't cross-checked case by case). Apropos today's other discussion: 7,520 people were aged 65+...9/n

...Conclusion? This is a far better report than the FDA's one on this vaccine: it's the "go to". Not comfortable that the unadjudicated person with severe Covid signals a bigger issue, but very glad the EMA is on it. 10/10